

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
23 November 2000 (23.11.2000)

PCT

(10) International Publication Number
WO 00/70095 A3

(51) International Patent Classification?: **C12Q 1/68**

(74) Agents: RUSZALA, Lois, K.; Dade Behring Inc., 1717 Deerfield Road, Deerfield, IL 60015 et al. (US).

(21) International Application Number: **PCT/US00/13526**

(81) Designated States (national): CA, JP.

(22) International Filing Date: 16 May 2000 (16.05.2000)

(84) Designated States (regional): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/313,240 17 May 1999 (17.05.1999) US
Published:
— with international search report

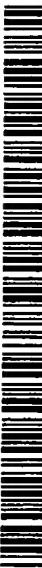
(71) Applicant: DADE BEHRING INC. [US/US]; 1717 Deerfield Road, Deerfield, IL 60015 (US).

(72) Inventors: KURN, Nurith; 2876 Ramona, Palo Alto, CA 94306 (US). LIU, Yen, Ping; 11525 Sunset Spring Court, Cupertino, CA 95014 (US).

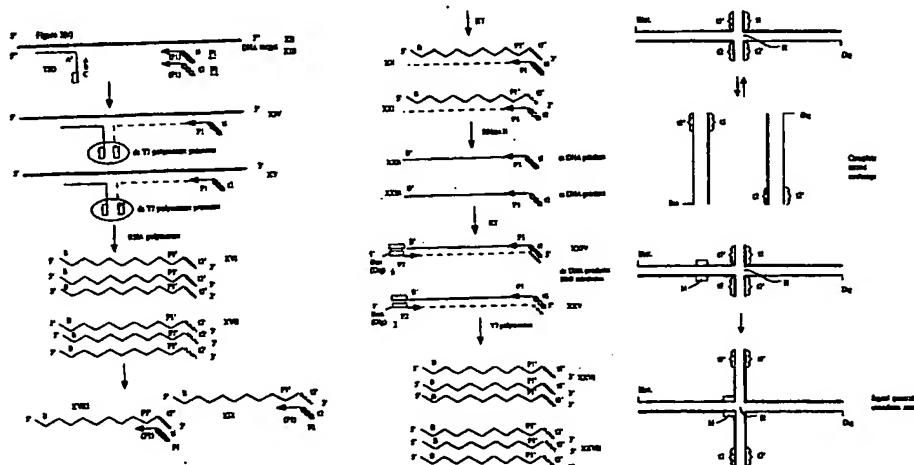
(88) Date of publication of the international search report:
2 August 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: HOMOGENEOUS ISOTHERMAL AMPLIFICATION AND DETECTION OF NUCLEIC ACIDS USING A TEMPLATE SWITCH OLIGONUCLEOTIDE



WO 00/70095 A3



(57) Abstract: An isothermal, transcription-based nucleic acid amplification method based on the formation of a target-dependent nucleic acid species by template switching. This product species can be amplified further to produce multiple copies of both double stranded DNA products and single stranded RNA product. The single stranded RNA amplification products are the same sense as the target sequence. Also provided is a branch migration inhibition based procedure for scanning nucleic acid sequences using the strand switch isothermal amplification. A template switch oligonucleotide used in the amplification includes a 3' region capable of hybridizing to a target sequence and a 5' region which does not hybridize to the target. The 5' region includes a promoter sequence of DNA dependent RNA polymerase. A first primer and a second primer may be used during amplification and detection. The first primer is capable of hybridizing to the target and the second primer is not target dependent. For detection, either the first primer or the second primer has a label.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/13526

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 24455 A (CLONTECH LAB INC) 10 July 1997 (1997-07-10) see whole doc. esp. claims and examples ---	1,2, 8-10,13; 16-18, 24,25,28
A	PATEL R. ET AL.,: "Formation of chimeric DNA primer extension products by template switching onto an annealed downstream oligonucleotide" PROC. NATL. ACAD. SCI, USA, vol. 93, - April 1996 (1996-04) pages 2969-2974, XP002158856 cited in the application the whole document --- -/-	1-51

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

30 January 2001

Date of mailing of the international search report

22/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl
Fax: (+31-70) 340-3016

Authorized officer

Mueller, F

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 00/13526

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 23646 A (BEHRINGERWERKE AG ;ULLMAN EDWIN F (US)) 3 July 1997 (1997-07-03) cited in the application the whole document ---	1-51
A	PANYUTIN I G ET AL: "FORMATION OF A SINGLE BASE MISMATCH IMPEDES SPONTANEOUS DNA BRANCH MIGRATION" JOURNAL OF MOLECULAR BIOLOGY, GB, LONDON, vol. 230, no. 2, 20 March 1993 (1993-03-20), pages 413-424, XP000673372 ISSN: 0022-2836 cited in the application the whole document ---	1-51
A	US 5 545 522 A (BARCHAS JACK D ET AL) 13 August 1996 (1996-08-13) the whole document ---	1-51

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/13526

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9724455	A 10-07-1997	US EP JP US	5962271 A 0871780 A 2000502905 T 5962272 A	05-10-1999 21-10-1998 14-03-2000 05-10-1999
WO 9723646	A 03-07-1997	AU EP US	1565397 A 0920532 A 6013439 A	17-07-1997 09-06-1999 11-01-2000
US 5545522	A 13-08-1996	US US	5716785 A 5891636 A	10-02-1998 06-04-1999